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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/652,978	02/08/91	BUHR C	4610-0027

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EXAMINER	
KUNZ, G	

ART UNIT	PAPER NUMBER
1803	11

DATE MAILED: 11/25/92

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 2/8/91 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1 – 26 are pending in the application.
   Of the above, claims 1-6, 19, 21, AND 23-26 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 7-18, 20, AND 22 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

This communication is a response to applicant's election without traverse of Group II, claims 7 - 18, 20 and 22, filed August 31, 1992.

Claims 1 - 6, 19, 21, and 23 - 26 stand withdrawn because they are directed to the non-elected invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 7 is rejected under 35 USC 102(b) as being anticipated by Padyukova et al. (Tetrahedron Letters 28: 3623 - 3626, 1987). Padyukova et al. discloses both uridine and adenosine 5'-methylene phosphonate on page 3624, compounds 13 and 14. These compounds read on claim 5 when Y and X are oxygen, R1 is hydroxyl, and B is uracil and adenine, respectively.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this

section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 8 - 9, 11 - 12, 14 - 16 and 18 are rejected under 35 USC 103 as being obvious over Robins et al. (J. Org. Chem. 39: 1564 - 1570) or Balzarini et al. (Mol. Pharm. 32: 162 - 167, 1987) or Ranganathan (Tetrahedron Letters 15: 1291 - 1294, 1977) or Martin et al. (J. Med. Chem. 33: 2137 - 2145, 1990) in view of Khorlin et al. (5,043,437).

Robins et al. discloses 2',3'-epoxynucleosides of adenosine related to the compound of claim 8 (page 1565, compound 3).

Balzarini et al. discloses 2',3'-didehydro-2',3'-dideoxy-cytidine related to the compound of claim 9.

Martin et al. discloses 2'-deoxy-2'-fluoro-cytidine (cmpd 17), 2'-fluoro-thymidine (cmpd 42), and 2'-deoxy-2'-fluoro-ara-cytidine (compd. 9) related to the compounds of claims 16, 18, and 12, respectively.

Ranganathan discloses 2'-deoxy-2'-fluoro-adenosine (page 1293, cmpd X) and 2'-deoxy-2'-fluoro-ara-adenosine (page 1293, cmpd XV).

The differences between the nucleoside analogs disclosed by the above references and the claimed nucleoside derivatives is the presence of the 5'-phosphonate moiety. However, Khorlin et al. discloses 5'-phosphonates of AZT to be derivatives that retain the anti-HIV activity of AZT but also possess reduced toxicity (see Tables 3 - 5). The claimed 5'-methylene

phosphonate derivatives of recognized antiviral nucleoside analogs would, therefore, have been obvious to the person of ordinary skill in the art wanting to create effective antiviral drugs with reduced toxicity over the traditional 5'-OH compounds. Thus, the claimed invention is prima facie obvious in the absence of clear and convincing evidence to the contrary.

Claims 20 and 22 are rejected under 35 USC 103 as being obvious over Padyukova et al. (Tetrahedron Letters 28: 3623 - 3626, 1987). As indicated supra, Padyukova et al. discloses both uridine and adenosine 5'-methylene phosphonates on page 3624. Claims 20 - 22 are directed to a composition of the 5'-methylene nucleoside phosphonates of claim 7 along with an inert pharmaceutical carrier. Such compositions are not patentable over a known active ingredient (Ex Parte Billman, 71 USPQ 253). The person of ordinary skill in the art at the time of the invention would have found such compositions of a known antiviral agent with a pharmaceutical carrier to have been obvious for the purpose of administering the active compound for even testing purposes. Thus, the claimed composition is prima facie obvious in the absence of clear and convincing evidence to the contrary.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains,

or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to provide an adequate written description and failing to teach adequately how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

The applicant is claiming hundreds of 5'-methylene phosphonate derivatives and alleges that they are all active antiviral compounds. However, the specifications provide not a single example of data supporting this allegation of antiviral efficacy. Without such data the applicant has not fulfilled his obligation to teach the person of ordinary skill in the art how to make and use the invention without undue experimentation.

Claims 7 - 18, 20 and 22 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 7 and 11 -13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is rendered indefinite because of the phrase "or modified form" because it is unclear what said modifications are.

Claim 7 is further indefinite because is not clear whether

both R1's must always be the same or if the applicant means to use to separate variables that can obviously vary independently.

Claims 11 - 13 are indefinite because there is no antecedent basis for "adenine", "cytosine", or "aziridinylcytosine" in claim 10 from which these claims depend.

The Disclosure Statement 1449 filed June 17, 1991 was apparently filed without accompanying copies of the references.

No claim is allowed.

Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kunz whose telephone number is (703) 308-3995.

G. K.
Gary L. Kunz:glk
November 16, 1992

Johnnie R. Brown
JOHNNIE R. BROWN
SUPERVISORY PATENT EXAMINER
ART UNIT 183